

In the claims:

Please amend claims 8-13, 17-20, 22, 23, and 30-33.

1. **(Original)** A method of treating a skin or nail disorder in a subject comprising administering to the subject a therapeutically effective amount of a neutralizing, high affinity TNF $\alpha$  antibody, such that said skin disorder or nail disorder is treated.
2. **(Original)** The method of claim 1, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof, that dissociates from human TNF $\alpha$  with a K<sub>d</sub> of  $1 \times 10^{-8}$  M or less and a K<sub>off</sub> rate constant of  $1 \times 10^{-3} \text{ s}^{-1}$  or less, both determined by surface plasmon resonance, and neutralizes human TNF $\alpha$  cytotoxicity in a standard *in vitro* L929 assay with an IC<sub>50</sub> of  $1 \times 10^{-7}$  M or less.
3. **(Original)** The method of claim 1, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof with the following characteristics:
  - a) dissociates from human TNF $\alpha$  with a K<sub>off</sub> rate constant of  $1 \times 10^{-3} \text{ s}^{-1}$  or less, as determined by surface plasmon resonance;
  - b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;
  - c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12.
4. **(Original)** The method of claim 1, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO:1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2.

5. **(Original)** The method of any one of claims 1, 2, 3, or 4, wherein the antibody is D2E7.

6. **(Original)** The method of any one of claims 1, 2, 3, or 4, wherein the skin disorder is selected from the group consisting of psoriasis, vulgaris, scleroderma, atopic dermatitis, sarcoidosis, erythema nodosum, hidradenitis suppurative, lichen planus, Sweet's syndrome, vitiligo, and suppurative folliculitis.

7. **(Original)** The method of claim 6, wherein psoriasis is selected from the group consisting of chronic plaque psoriasis, guttate psoriasis, inverse psoriasis, pustular psoriasis, vulgaris, erythrodermic psoriasis, psoriasis associated with inflammatory bowel disease (IBD), and psoriasis associated with rheumatoid arthritis (RA).

8. **(Currently amended)** A method of treating a subject suffering from a skin disorder comprising administering a therapeutically effective amount of a human TNF $\alpha$  antibody, or an antigen-binding fragment thereof, to the subject, wherein the antibody dissociates from human TNF $\alpha$  with a  $K_d$  of  $1 \times 10^{-8}$  M or less and a  $K_{off}$  rate constant of  $1 \times 10^{-3} s^{-1}$  or less, both determined by surface plasmon resonance, and neutralizes human TNF $\alpha$  cytotoxicity in a standard *in vitro* L929 assay with an  $IC_{50}$  of  $1 \times 10^{-7}$  M or less, such that the skin disorder is treated.

9. **(Currently amended)** A method of treating a subject suffering from an skin disorder comprising administering a therapeutically effective amount of a human TNF $\alpha$  antibody, or an antigen-binding fragment thereof, with the following characteristics:

- a) dissociates from human TNF $\alpha$  with a  $K_{off}$  rate constant of  $1 \times 10^{-3} s^{-1}$  or less, as determined by surface plasmon resonance;
- b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;
- c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9,

10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12, such that the skin disorder is treated.

10. **(Currently amended)** A method of treating a subject suffering from a skin disorder comprising administering a therapeutically effective amount of a human TNF $\alpha$  antibody, or an antigen-binding fragment thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2, such that the skin disorder is treated.

11. **(Currently amended)** A method of treating a subject suffering from a nail disorder comprising administering a therapeutically effective amount of a human TNF $\alpha$  antibody, or an antigen-binding fragment thereof, to the subject, wherein the antibody dissociates from human TNF $\alpha$  with a  $K_d$  of  $1 \times 10^{-8}$  M or less and a  $K_{off}$  rate constant of  $1 \times 10^{-3} s^{-1}$  or less, both determined by surface plasmon resonance, and neutralizes human TNF $\alpha$  cytotoxicity in a standard *in vitro* L929 assay with an  $IC_{50}$  of  $1 \times 10^{-7}$  M or less, such that the nail disorder is treated.

12. **(Currently amended)** A method of treating a subject suffering from a nail disorder comprising administering a therapeutically effective amount of a human TNF $\alpha$  antibody, or an antigen-binding fragment thereof, with the following characteristics:

- a) dissociates from human TNF $\alpha$  with a  $K_{off}$  rate constant of  $1 \times 10^{-3} s^{-1}$  or less, as determined by surface plasmon resonance;
- b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;
- c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12 such that the nail disorder is treated.

13. **(Currently amended)** A method of treating a subject suffering from a nail disorder comprising administering a therapeutically effective amount of a human TNF $\alpha$  antibody, or an antigen-binding fragment thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2 such that the nail disorder is treated.

14. **(Original)** The method of any one of claims 8 to 13, wherein the antibody, or antigen-binding fragment thereof, is D2E7.

15. **(Original)** The method of any one of claims 8, 9, or 10, wherein the skin disorder is selected from the group consisting of psoriasis, vulgaris, scleroderma, atopic dermatitis, sarcoidosis, erythema nodosum, hidradenitis suppurative, lichen planus, Sweet's syndrome, vitiligo, suppurative folliculitis, chronic actinic dermatitis, bullous pemphigoid, and alopecia areata.

16. **(Original)** The method of claim 15, wherein the psoriasis is selected from the group consisting of chronic plaque psoriasis, guttate psoriasis, inverse psoriasis, pustular psoriasis, vulgaris, erythrodermic psoriasis, psoriasis associated with inflammatory bowel disease (IBD), and psoriasis associated with rheumatoid arthritis (RA).

17. **(Currently amended)** A method of treating a subject suffering from psoriasis comprising administering a therapeutically effective amount of a human TNF $\alpha$  antibody, or an antigen-binding fragment thereof, to the subject, wherein the antibody dissociates from human TNF $\alpha$  with a  $K_d$  of  $1 \times 10^{-8}$  M or less and a  $K_{off}$  rate constant of  $1 \times 10^{-3} \text{ s}^{-1}$  or less, both determined by surface plasmon resonance, and neutralizes human TNF $\alpha$  cytotoxicity in a standard *in vitro* L929 assay with an  $IC_{50}$  of  $1 \times 10^{-7}$  M or less, such that said psoriasis is treated.

18. **(Currently amended)** A method of treating a subject suffering from psoriasis comprising administering a therapeutically effective amount of a human TNF $\alpha$  antibody, or an antigen-binding fragment thereof, with the following characteristics:

- a) dissociates from human TNF $\alpha$  with a  $K_{off}$  rate constant of  $1 \times 10^{-3} \text{ s}^{-1}$  or less, as determined by surface plasmon resonance;
- b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;
- c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12, such that said psoriasis is treated..

19. **(Currently amended)** A method of treating a subject suffering from psoriasis comprising administering a therapeutically effective amount of a human TNF $\alpha$  antibody, or an antigen-binding fragment thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2, such that said psoriasis is treated..

20. **(Currently amended)** The method of any one of claims 17, 18, or 19, wherein the TNF $\alpha$  antibody, or antigen binding fragment thereof, is D2E7.

21. **(Original)** The method of any one of claims 17, 18, or 19, wherein the psoriasis is selected from the group consisting of chronic plaque psoriasis, guttate psoriasis, inverse psoriasis, pustular psoriasis, vulgaris, erythrodermic psoriasis, psoriasis associated with inflammatory bowel disease (IBD), and psoriasis associated with rheumatoid arthritis (RA).

22. **(Currently amended)** The method of any one of claims 17, 18, or 19, wherein the TNF $\alpha$  antibody is administered with at least one additional therapeutic agent.

23. **(Currently amended)** A method for inhibiting human TNF $\alpha$  activity in a human subject suffering from an psoriasis comprising administering a therapeutically effective amount of a human TNF $\alpha$  antibody, or an antigen-binding fragment thereof, to the subject, wherein the antibody dissociates from human TNF $\alpha$  with a  $K_d$  of  $1 \times 10^{-8} \text{ M}$  or less and a  $K_{off}$  rate constant

of  $1 \times 10^{-3}$  s<sup>-1</sup> or less, both determined by surface plasmon resonance, and neutralizes human TNF $\alpha$  cytotoxicity in a standard *in vitro* L929 assay with an IC<sub>50</sub> of  $1 \times 10^{-7}$  M or less.

24. **(Original)** The method of claim 23, wherein the psoriasis is selected from the group consisting of chronic plaque psoriasis, guttate psoriasis, inverse psoriasis, pustular psoriasis, vulgaris, erythrodermic psoriasis, psoriasis associated with inflammatory bowel disease (IBD), and psoriasis associated with rheumatoid arthritis (RA).

25. **(Original)** A method of treating a subject suffering from a skin disorder comprising administering a therapeutically effective amount of D2E7, or an antigen-binding fragment thereof, to the subject, such that the disease is treated.

26. **(Original)** The method of claim 25, wherein the skin disorder is selected from the group consisting of psoriasis, vulgaris, scleroderma, atopic dermatitis, sarcoidosis, erythema nodosum, hidradenitis suppurative, lichen planus, Sweet's syndrome, vitiligo, and suppurative folliculitis, chronic actinic dermatitis, bullous pemphigoid, and alopecia areata.

27. **(Original)** The method of claim 26, wherein the psoriasis is selected from the group consisting of chronic plaque psoriasis, guttate psoriasis, inverse psoriasis, pustular psoriasis, vulgaris, erythrodermic psoriasis, psoriasis associated with inflammatory bowel disease (IBD), and psoriasis associated with rheumatoid arthritis (RA).

28. **(Original)** A method of treating a subject suffering from a nail disorder comprising administering a therapeutically effective amount of D2E7, or an antigen-binding fragment thereof, to the subject, such that the disorder is treated.

29. **(Original)** A method of treating a subject suffering from psoriasis selected from the group consisting of chronic plaque psoriasis, psoriasis associated with inflammatory bowel disease (IBD), and psoriasis associated with rheumatoid arthritis (RA), comprising administering a therapeutically effective amount of D2E7, or an antigen-binding fragment thereof, to the subject, such that the psoriasis is treated.

30. **(Currently amended)** A kit comprising:

a) a pharmaceutical composition comprising a human TNF $\alpha$ -antibody, or an antigen binding portion thereof, and a pharmaceutically acceptable carrier, wherein the antibody dissociates from human TNF $\alpha$  with a K<sub>d</sub> of 1 x 10<sup>-8</sup> M or less and a K<sub>off</sub> rate constant of 1 x 10<sup>-3 s<sup>-1</sup></sup> or less, both determined by surface plasmon resonance, and neutralizes human TNF $\alpha$  cytotoxicity in a standard *in vitro* L929 assay with an IC<sub>50</sub> of 1 x 10<sup>-7</sup> M or less; and

b) instructions for administering to a subject the TNF $\alpha$  antibody pharmaceutical composition for treating a subject who is suffering from psoriasis.

31. **(Currently amended)** A kit comprising:

a) a pharmaceutical composition comprising a human TNF $\alpha$ -antibody, or an antigen binding portion thereof, and a pharmaceutically acceptable carrier, wherein the antibody dissociates from human TNF $\alpha$  with a K<sub>d</sub> of 1 x 10<sup>-8</sup> M or less and a K<sub>off</sub> rate constant of 1 x 10<sup>-3 s<sup>-1</sup></sup> or less, both determined by surface plasmon resonance, and neutralizes human TNF $\alpha$  cytotoxicity in a standard *in vitro* L929 assay with an IC<sub>50</sub> of 1 x 10<sup>-7</sup> M or less; and

b) instructions for administering to a subject the TNF $\alpha$  antibody pharmaceutical composition for treating a subject who is suffering from a chronic plaque psoriasis.

32. **(Currently amended)** A kit comprising:

a) a pharmaceutical composition comprising a human TNF $\alpha$ -antibody, or an antigen binding portion thereof, and a pharmaceutically acceptable carrier, wherein the antibody dissociates from human TNF $\alpha$  with a K<sub>d</sub> of 1 x 10<sup>-8</sup> M or less and a K<sub>off</sub> rate constant of 1 x 10<sup>-3 s<sup>-1</sup></sup> or less, both determined by surface plasmon resonance, and neutralizes human TNF $\alpha$  cytotoxicity in a standard *in vitro* L929 assay with an IC<sub>50</sub> of 1 x 10<sup>-7</sup> M or less; and

b) instructions for administering to a subject the TNF $\alpha$  antibody pharmaceutical composition for treating a subject who is suffering from nail disorder.

33. **(Currently amended)** A kit according to any one of claims 30, 31, or 32, wherein the TNF $\alpha$  antibody, or an antigen binding portion thereof, is D2E7.